REMARKS

Claims 1 and 3 have been amended. Claims 8, 9, and 12-20 have been canceled without prejudice. Claims 4 and 21-24 are withdrawn. Claim 1 has been amended to incorporate features of claims 8 and 9. Claim 3 has been amended for clarity. Upon entry of this amendment, claims 1-3, 5-7, 10, and 11 will be pending and under examination.

The specification has been amended to correct the description of Figure 2 at page 4, line 32, to page 5, line 9, to delete a redundant phrase, and insert commas. More specifically, the phrase "vaccine + chemotherapy" at page 5, lines 8-9, has been replaced with "chemotherapy," so that the sentence states: "Survival of the vaccine group tended to be lower, but was not statistically different, than that of the chemotherapy group (p=0.05, log-rank)." This amendment is supported by Figure 2 as originally filed, and by the description of Figure 2 in Examples 1 and 2. Figure 2 and the specification at page 13, lines 10-13, indicate that the difference in survival between chemotherapy and vaccinated patients was not significantly different. Figure 2 and the specification at page 13, lines 27-28, indicate that survival of patients receiving vaccination and chemotherapy exhibited significantly prolonged survival relative to those receiving either treatment individually. No new matter has been added.

The following remarks are in response to the Office Action mailed October 18, 2007 ("the Office Action").

Objection to the Specification

The disclosure was objected to at pages 2-3 of the Office Action because

> there appears to be incongruent statements on page 5, lines 5-9…It is unclear how the survival of the vaccine + chemotherapy group can be significantly greater than both other groups…at the same time the vaccine group is not statistically different from the vaccine + chemotherapy group.

This objection is met by the amendment to the specification to correct the description of Figure 2 at pages 4-5. As amended, the description states that survival of the vaccine + chemotherapy group is significantly greater than both other groups, and that survival in the

vaccine group is not statistically different from the chemotherapy group. Applicants request withdrawal of this objection.

35 U.S.C. § 112, second paragraph

Claims 3 and 14 were rejected as indefinite because "it is unclear if the adjective 'autologous' is intended to describe the tumor antigen, the DC itself, or both." Claim 3, as amended, more clearly indicates that the DC are autologous, and that the DC are tumor antigen-presented DC. Applicants request withdrawal of this rejection.

35 U.S.C. § 102

Tong et al. (Cancer Research, 61:7530-7535, 2001; "Tong")

Claims 1, 5, 6, 12, 16, and 17 were rejected as allegedly anticipated by Tong. The Office Action stated (pages 4-5):

> Tong et al. teach a method for treating cancer in a mammal (mouse) comprising administering four separate injections of DC with each injection at an amount of 10^6 DC, subsequent to three treatments of chemotherapy…Tong et al. teach that the combination of chemotherapy with DC treatment markedly enhanced survival of mice with tumors as compared to mice treated with chemotherapy or DC alone…[T]he method taught by the prior art comprises the same method steps of providing at least one vaccination of DC to said mammal as recited in the claimed method, hence the method taught by the prior art would increase chemosensitivity of a mammal.

Claims 12, 16, and 17 have been canceled. Claim 1 has been amended to incorporate features of claims 8 and 9, which were not included in the rejection. Claim 1, as amended, is drawn to a method for treating a disease condition in a mammal by administering at least one vaccination of dendritic cells ("DC") to the mammal; and administering a regimen of chemotherapy to the mammal, wherein at least one vaccination of DC occurs prior to administering the regimen of chemotherapy, and wherein the regimen of chemotherapy includes the administration of at least one chemotherapeutic agent selected from the group consisting of temozolomide, procarbazine, carboplatin, vincristine, BCNU, CCNU, thalidomide, irinotecan, isotretinoin, imatinib, etoposide, and combinations thereof. Claims 5 and 6 depend from claim 1.

Tong does not disclose a method for treating a mammal in which at least one vaccination of DC occurs prior to administering the regimen of chemotherapy. Rather, Tong discloses a method in which administration of DC was started only after chemotherapy (see Tong at page 7531, right column, sixth full paragraph). Tong also does not disclose a method in which chemotherapy includes the administration of at least one chemotherapeutic agent selected from the group consisting of temozolomide, procarbazine, carboplatin, vincristine, BCNU, CCNU, thalidomide, irinotecan, isotretinoin, imatinib, etoposide, and combinations thereof. Thus, Tong does not disclose all of the elements of claim 1, and the rejection of claims 1, 5, and 6, as allegedly anticipated by Tong, should be withdrawn.

Yu et al. I (Cancer Research, 61:842-847, 2001; "Yu I")

Claims 12-14, 16, 17, 19, and 20 were rejected as allegedly anticipated by Yu I. Applicants have obviated this rejection by cancelling claims 12-20 without prejudice.

Vitiello et al. (U.S. Pat. Pub. No. 2002/0119121; "Vitiello")

Claims 1-3, 8, 10-14, 19, and 20 were rejected as allegedly anticipated by Vitiello. The Office Action stated (page 7):

> Vitiello et al. teach a method of treating cancer in a patient (mammalian) comprising administering DC to a patient prior to, during, or subsequent to chemotherapy treatment...wherein the DC are autologous and primed ex vivo with tumor antigens from the patient...wherein the cancer is glioblastoma multiforme.

Claims 12-20 have been canceled. Claim 1 has been amended to include features of claims 8 and 9. Claim 1 recites a method for treating a disease condition including administering at least one vaccination of DC and administering a chemotherapy regimen. The chemotherapy regimen includes the administration of at least one chemotherapeutic agent selected from the group consisting of temozolomide, procarbazine, carboplatin, vincristine, BCNU, CCNU, thalidomide, irinotecan, isotretinoin, imatinib, etoposide, and combinations thereof. Vitiello does not disclose regimens with any of temozolomide, procarbazine, carboplatin, vincristine, BCNU, CCNU, thalidomide, irinotecan, isotretinoin, imatinib, and etoposide. As Vitiello does

not mention these agents, the reference does not anticipate claims 1-3, 8, and 10-12. Withdrawal of this rejection is requested.

Yu et al. II (U.S. Pat. Pub. No. 2004/0057935; "Yu II")

Claims 1-3, 5-7, 10-14, and 16-20, were rejected as allegedly anticipated by Yu II because "Yu et al. II teach a method of treating cancer comprising administering DC to a patient (mammalian) ([2-12]; [15-19]; [24-25]; Examples 1-9), wherein the DC can be autologous and primed *ex vivo* with a tumor antigen before administration to the patient ([9-10]; [27])" (page 9).

Claim 1, as amended, includes features of both claims 8 and 9. Claim 1 recites a method for treating a disease condition including administering at least one vaccination of DC and administering a chemotherapy regimen. The chemotherapy regimen includes administration of at least one of temozolomide, procarbazine, carboplatin, vincristine, BCNU, CCNU, thalidomide, irinotecan, isotretinoin, imatinib, etoposide, and combinations thereof. Yu II does not disclose the specific chemotherapeutic agents recited in claim1. Thus, Yu II does not anticipate claims 1-3, 5-7, or 10-14.

35 U.S.C. § 103

Yu II in view of Friedman et al. (Clin. Cancer Res., 6:2585-2597, 2000; "Friedman")

Claims 1 and 9 were rejected as allegedly unpatentable over Yu II (discussed above regarding § 102) in view of Friedman.

As noted by the Examiner, a rejection under § 103(a) may be overcome if the cited reference, Yu II, is disqualified under § 103(c). The availability of Yu II as a reference is premised on § 102(e). 35 U.S.C. § 103(c) provides that subject matter citable as prior art under § 102(e) is not to be considered in determining whether an invention sought to be patented is obvious under 35 U.S.C. § 103, provided the subject matter and the claimed invention were commonly owned at the time the invention was made. See also 37 C.F.R. § 1.104(c)(4). Both the Yu II and the present application are assigned to Cedars-Sinai Medical Center. The assignment for Yu II is recorded at reel/frame 020375/0751. At the time the claimed invention

was made, it was subject to an obligation of assignment to Cedars-Sinai Medical Center. The assignment for the present application is recorded at reel/frame 017797/0031. Given that the present application and Yu II are owned by the same entity, Yu II cannot be cited against the claims of the present application under 35 U.S.C. § 103 and 37 C.F.R. § 1.104(c)(4).

Friedman was cited to supplement Yu II because it discloses "successful treatment of glioblastoma multiforme in patients comprising administering temozolomide" (Office Action at page 11). Friedman does not disclose methods for treating a mammal that include administering vaccination of DC, and Yu II is not citable against the claims for reasons stated above. Thus, the claims are patentable over Friedman. Withdrawal of this rejection is respectfully requested.

Vitiello in view of Friedman

Claims 1 and 9 were rejected as unpatentable over Vitiello (discussed above regarding § 102) in view of Friedman. According to the Office Action (page 13),

> One would have been motivated to use temozolomide as the chemotherapeutic in the method taught be Vitiello et al. because Friedman et al. demonstrate that temozolomide successfully and safely treats glioblastoma multiforme and expressly suggests combining temozolomide with other agents that use different cytotoxic mechanisms to produce cytotoxic effects. One of ordinary skill in the art would have a reasonable expectation of success treating glioblastoma multiforme with DC and temozolomide because both agents are known to treat glioblastoma multiforme.

This rejection is respectfully traversed. Applicants disagree that claim 1 is prima facie obvious over Vitiello in view of Friedman (claim 9 has been canceled). Claim 1 recites a method for treating a disease condition including administering at least one vaccination of DC prior to administering a chemotherapy regimen.

First of all, this rejection appears to assume that Vitiello discloses all limitations of claim 1 except for chemotherapy with temozolomide. To the contrary, Vitiello does not describe a method for treating a disease condition in a mammal by administering at least one vaccination of DC prior to administering a regimen of chemotherapy. The disclosure of Vitiello primarily concerns methods of inducing $CD8^+$ T lymphocytes ex vivo, and treating patients by

administering the T lymphocytes (see Vitiello, e.g., in the Summary of the Invention, and the claims). Vitiello refers to chemotherapy in two passages. At paragraph [0004], Vitiello describes the unsuitability of chemotherapy, noting that it "can cause substantial damage to normal tissue in the treatment field, resulting in scarring and in severe cases, loss of function of normal tissue." At paragraph [0135], Vitiello states that "for treating cancer, the methods of the invention can be practiced prior to, during, or subsequent to conventional cancer treatments such as surgery, chemotherapy, including administration of cytokines and growth factors, radiation or other methods known in the art." Neither passage suggests methods in which a mammal is administered chemotherapy after DC. Vitiello discusses administration of CTLs "with conventional therapy" at paragraph [0139], and then proceeds to discuss DC vaccination in paragraph [0140] as "[a]nother application of this invention." Vitiello provides no suggestion to practice DC vaccination in conjunction with "conventional therapy," much less with a chemotherapeutic treatment regimen.

Second of all, Friedman does not contain any suggestion to use temozolomide in conjunction with a cell-based therapeutic treatment, much less DC administration. Friedman refers to combination regiments that include treatment with cisplatin, BCNU, and interferon-alpha-2b. None of these treatment regimens bear any resemblance to DC administration, and cannot be said to suggest the claimed methods.

For at least the reasons given above, the Office has failed to establish a prima facie case of obviousness. Furthermore, applicants respectfully note the objective evidence of nonobviousness set forth in the specification. As described in the Examples, a trial was conducted in which glioblastoma multiforme (GBM) patients were treated with DC vaccination, chemotherapy, or DC vaccination followed by chemotherapy. GBM patients receiving chemotherapy after vaccination enjoyed significantly delayed tumor progression and significantly prolonged survival relative to patients receiving either treatment individually (specification, page 13, paragraph [0045]). Notably, post-vaccination chemotherapy resulted in a substantial increase (42%) in 2-year survivors (specification, page 14, paragraph [0046]). No 3- or 4-year survivors were evident after chemotherapy or vaccination alone, but post-vaccine

chemotherapy patients included both 3- and 4- year survivors (specification, page 14, paragraph [0046]). In addition, tumor regression was observed in patients receiving the vaccine and chemotherapy treatment. This was the first demonstration of objective regression in an adoptive immunotherapy setting (specification, page 14, paragraph [0047]). These observed clinical benefits, which are thought to result from increased chemosensitivity induced by DC administration, markedly surpass those in previous vaccine studies and GBM chemotherapy studies (specification, page 15, paragraph [0048]). The claimed methods provide significant benefits not taught or suggested by the cited references. In view of the foregoing, applicants request withdrawal of the rejection of claim 1 as obvious over Vitiello in view of Friedman.

CONCLUSION

Applicants submit that the claims are in condition for allowance and such action is requested. A Petition for Extension of Time and required fee is being filed herewith. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket no. 22862-004US1.

Respectfully submitted,

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